## REMARKS

After entry of this amendment, claims 2, 4, 5, 32, 34, 35, 37, 38 and 40-42 are pending. Claims 33, 36, 39 and 43 have been cancelled without prejudice or disclaimer. The claims have been amended without prejudice or disclaimer and find support *inter alia* in the original claims. Claim 2 finds further support in the specification, for example, at page 32, lines 5-6. Claim 35 finds further support in the specification, for example, at page 20, lines 35-39, and page 32, lines 5-6. Claim 40 finds further support in the specification, for example, at page 20, lines 35-39. No new matter has been added.

## Claim Objection

Claims 39 and 43 are objected to as being of improper dependent form for allegedly failing to further limit the subject matter of a previous claim, i.e. claims 2 and 35, respectively. Applicants respectfully disagree. However, to expedite prosecution, claims 39 and 43 have been cancelled without prejudice or disclaimer. Applicants believe that the present amendment renders the objection moot. Accordingly, withdrawal of the objection is respectfully requested.

## Claim Rejection – 35 U.S.C. § 112

### *Enablement Rejection*

Claims 2, 4, 5, 32, 33, 38 and 39 are rejected under 35 U.S.C. § 112, first paragraph, for allegedly lacking an enabling disclosure.

The Examiner alleges that the specification is enabling only for a process for the production of fine chemical comprising increasing or generating the expression of the recited nucleic acid molecule in a plant or a part thereof but not the same process in any other types of organisms or their parts. The Examiner asserts that the specification does not disclose the recovery of at least one fine chemical produced by the other organisms or their parts subsequent to the transformation with the claimed nucleic acid molecule. The Examiner further contends that the types of fine chemicals that would be produced by organisms other than plants subsequent to the transformation cannot be predicted based on the results obtained from plants. For support, the Examiner cites to Valster *et al.* (hereinafter "Valster") and Zheng *et al.* (hereinafter "Zheng") for the alleged proposition that plant cells differ from other types of cells with respect to how RHO GTPase are regulated and function within them. Applicants

respectfully disagree. However, to expedite prosecution, the claims have been amended without prejudice or disclaimer to recite the claimed subject matter with more specificity. Applicants submit that the claims as amended overcome the rejection for the following reasons.

It is noted initially that, as amended, claim 2 further specifies that the organism is a bacterium, an algae, or a plant. It is further noted that bacteria and algae are routinely used in the art for production of chemicals such as proteins. Thus, methods for recovery chemicals from those single-celled organisms are well known and routine to one skilled in the art. Because the information is already available in the art, the law does not set a *per se* rule that such information must be determined afresh. *See Capon v. Eshhar*, 418 F.3d 1349, 1358, 1357 (Fed. Cir. 2005). For at least this reason, Applicants submit that the specification, in view of the knowledge of the art, enables one of ordinary skill in the art to make and/or use the claimed subject matter as amended without the need of undue experimentation.

Moreover, Applicants further submit that the cited Valster and Zheng references do not support the Examiner's assertion of unpredictability at least to the extent that the amended claims are concerned. Both Valster and Zheng disclose small GTP-binding proteins of the Rho family from plants. Based on phylogenetic analysis, the Rho family is further divided into four subfamilies: Rop, Cdc42, Rac, and Rho subfamilies. See Valster at page 142, Figure 1. As noted by the Examiner, Valster concludes the plant Rho GTPases (Rops) as being distant cousins, rather than near siblings, of the GTPases in the Rho/Rac/Cdc42 subfamilies in other eukaryotes and they could be subject to different control mechanisms. Valster at page 146, left Col., 1st paragraph. Applicants note that the aforementioned conclusion made by Valster was based on a comparison between plant Rho GTPases and Rho GTPases from animal and fungus. Similarly, Zheng describes the plant Rop GTPases as being an important signaling switch in plant signal transduction. Comparisons as to the structure and the potential roles of these GTPases are made primarily between plant Rho GTPases and Rho GTPases from animal. Thus, it is clear that neither Valster nor Zheng supports the Examiner's assertion of unpredictability and thus, the conclusion of nonenablement at least to the extent the present claims as amended are concerned.

For at least the above reasons and further in view of the present amendment, Applicants respectfully request reconsideration and withdrawal of the rejection.

***Indefiniteness Rejection***

Claims 2 and 35, and claims 4, 5, 32-34, 36-38 and 40-42 dependent therefrom, are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite in light of claims 39 and 43. Applicants disagree and traverse the rejection. Without acquiescing to the merits of the Examiner's argument and solely for expediting prosecution, claims 39 and 43 have been cancelled without prejudice or disclaimer. Applicants believe that the present amendment overcomes the rejection. Reconsideration and withdrawal of the rejection is therefore respectfully requested.

**Claim Rejection – 35 U.S.C. § 103**

Claims 35-37 and 40-43 are rejected under 35 U.S.C. § 103(a) as being obvious over Qadota *et al.* (hereinafter "Qadota"), in view of Polashock *et al.* (hereinafter "Polashock"), Colau *et al.* (hereinafter "Colau"), Hamill *et al.* (hereinafter "Hamill"), Von Schaewen *et al.* (hereinafter "Von Schaewen"), Londesborough *et al.* (hereinafter "Londesborough"), and Hunt *et al.* (hereinafter "Hunt").

The Examiner relies on Qadota for allegedly teaching a process comprising stably increasing or generating the expression of SEQ ID NO: 1 in yeast, a nucleic acid molecule obtained from yeast. According to the Examiner, the introduction and expression of the nucleic acid molecule in the process taught by Qadota confers an increase in the amount of a fine chemical, i.e. the RAS2 protein, in yeast. The Examiner acknowledges that Qadota does not teach expression of the nucleic acid molecule in a plant, but relies on Polashock, Colau, Hamill, Von Schaewen, Londesborough, and Hunt for such teaching. Specifically, the Examiner asserts that all the cited secondary references teach expression of a nucleic acid molecule obtained from yeast in plants, which confers an increase of the amount of a fine chemical (e.g., protein encoded by the nucleic acid molecule). The Examiner alleges that it would have been obvious to express in plants any known nucleic acid molecule obtained from yeast, including that of SEQ ID NO: 1, because it would be a simple substitution of equivalent elements to obtain predictable results. The Examiner further contends that any additional effects, such as production of specific fine chemicals recited in the claims, would be inherent to such an expression of the nucleic acid molecule and the encoded protein. Applicants strongly disagree with the Examiner's above assertions and the finding of obviousness for the following reasons.

The Examiner bears the initial burden of establishing *prima facie* obviousness. *See In re Rijckaert*, 9 F.3d 1531, 1532, 28 USPQ2d 1955, 1956 (Fed. Cir. 1993). To support a *prima facie* conclusion of obviousness, the prior art must disclose or suggest all the limitations of the claimed invention. *See In re Lowry*, 32 F.3d 1579, 1582, 32 USPQ2d 1031, 1034 (Fed. Cir. 1994).

As noted by the Examiner, Qadota discloses a process comprising stably increasing or generating the expression of the RHO2 gene, a nucleic acid molecule obtained from yeast, in yeast. However, contrary to the Examiner's assertion, Qadota does not teach that the introduction and expression of this RHO2 nucleic acid molecule confers an increase in the amount of the RAS2 protein, the alleged fine chemical, in yeast. Rather, as demonstrated in Figure 3 at page 739 of Qadota, the production of the RAS2 protein is due to the introduction and expression of the RAS2 gene. As shown in Figure 3, all strains transformed with the pKS87 plasmid, which contains the RAS2 gene under the control of the galactose-inducable GAL1 promoter, produce the RAS2 protein. See e.g., lanes 1 and 4-7 of Figure 3 and page 736, left Col., 1st paragraph. Among those RAS2-producing yeast strains, only the strain used in lane 7 was transformed with the RHO2 gene. Thus, it is clear that the introduction and expression of the RHO2 gene does not confer the production of the alleged fine chemical, i.e. the RAS2 protein, as asserted by the Examiner. Nor does Qadota show that introduction and expression of the RHO2 gene confer the production of any fine chemical other than the encoded protein.

The combination of Qadota with Polashock, Colau, Hamill, Von Schaewen, Londesborough, and/or Hunt does not remedy this deficiency. As characterized by the Examiner, each of the Polashock, Colau, Hamill, Von Schaewen, Londesborough, and Hunt references teaches transforming and expressing a nucleic acid molecule obtained from yeast in plants, which in turn produces the encoded protein in plants. None of the nucleic acid molecules used in the cited secondary references relates to plant Rho GTPases. None of the cited secondary references teaches or suggests expression of the yeast RHO2 protein in plants would confer the production of a fine chemical, let alone the production of the RAS2 protein. Thus, it is clear that the combination of Qadota with Polashock, Colau, Hamill, Von Schaewen, Londesborough, and/or Hunt does not teach or suggest all of the claim limitations and thus, a *prima facie* case of obviousness has not been established. Accordingly, the rejection should be withdrawn for this reason alone.

Moreover, it is well established that under 35 U.S.C. § 103 the Examiner cannot selectively pick and choose from the disclosed parameters without proper motivation as to a particular selection. The mere fact that a reference may be modified to reflect features of the claimed invention does not make the modification, and hence the claimed invention, obvious unless the prior art suggested the desirability of such modification. *In re Mills*, 916 F.2d 680, 682, 16 USPQ2d 1430 (Fed. Cir. 1990); *In re Fritch*, 23 USPQ2d 1780 (Fed. Cir. 1992). "[A] patent composed of several elements is not proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art . . . it can be important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements ***in the way the claimed new invention does***." *See KSR International Co. v. Teleflex Inc.*, 82 USPQ2d 1385, 1396 (2007) (emphasis added).

It is noted initially that the Examiner's above reasoning in finding motivation and reasonable expectation of success is partially, if not wholly, based on an assumption that any yeast gene may be expressed in plants and such expression would then result in the production of a fine chemical, such as the protein encoded by the introduced yeast gene. Applicants strongly disagree.

As an initial matter, Applicants wish to draw the Examiner's attention to the recitation concerning "fine chemical" in claim 2, where it defines "fine chemical" as being "selected from the group consisting of amino acids, carbohydrates, vitamins, organic acids, fatty acids, and carotenoids." "Amino acids" include essential amino acids, non-essential amino acids, or modified amino acids, but not proteins. Thus, the production of the protein encoded by the yeast gene introduced into a plant cannot be considered as the production of a fine chemical as required by the claims.

Moreover, Applicants wish to note that in the cited secondary references, one skilled in the art would have had a reasonable expectation that the alleged "fine chemical," other than the encoded protein, would be produced because of the known function of the encoded protein. For example, in Polashock, a yeast Δ-9 fatty acid desaturase was introduced and expressed in plants and the transgenic plants were shown to produce increased amount of fatty acids. This is predictable because the yeast gene introduced into the plants, the Δ-9 fatty acid desaturase gene, was known to be involved in fatty acid biosynthesis. Similarly, in Hamill, a yeast ornithine

decarboxylase was introduced and expressed in plants and the transgenic plants were shown to produce increased amount of putrescine and nicotine. This is predictable because the yeast gene introduced into the plants, the yeast ornithine decarboxylase, was known to be involved in the pathway leading to the formation of putrescine and nicotine. See Hamill at page 28, Figure 1. Likewise, in Londesborough, a yeast trehalose synthase was introduced and expressed in plants and the transgenic plants were shown to produce increased amount of trehalose. This is predictable because the yeast gene introduced into the plants, the yeast trehalose synthase, was known to be involved in the biosynthesis of trehalose. However, this is not the case when the yeast RHO gene is introduced into plants.

As described in the specification, the yeast RHO gene as shown in SEQ ID NO: 1 encodes a protein that may play a role in the establishment of cell polarity or in microtubule assembly. See Specification at page 11, lines 5-12. Thus, it is clear that the function of the RHO protein is not well defined and the RHO protein is likely not involved in a specific biosynthesis or metabolism pathway. Accordingly, one skilled in the art would not have had a reasonable expectation of success that introduction and expression of a yeast RHO gene in plants would confer an increase in the amount of a fine chemical that is not the encoded protein. Absent such a reasonable expectation of success, there would be no motivation for one skilled in the art to introduce and express the yeast RHO gene, such as that shown in SEQ ID NO: 1, in plants as suggested by the Examiner. Accordingly, the rejection should be withdrawn for this additional reason.

Additionally, Applicants note that, in making the present rejection, the Examiner further alleges that any additional effects, such as production of specific fine chemicals, would be inherent to the expression of the nucleic acid molecule and the encoded protein. Applicants strongly disagree with the Examiner's application of inherency in the context of this obviousness rejection.

It is well established that inherency of missing features/limitations is limited to the context of anticipation under 35 U.S.C. § 102. In other words, obviousness under 35 U.S.C. § 103(a) cannot be established through inherency. Moreover, to establish that a missing claim limitation is inherent, the Examiner must provide rationale or evidence making "clear that the missing descriptive matter is necessarily present in the thing described in the reference." *In re*

*Robertson*, 169 F.3d 743, 745 (Fed. Cir. 1999). As such, inherency may not be established by probabilities or possibilities and "[t]he mere fact that a certain thing may result from a given set of circumstances is not sufficient [to establish inherency]." *See In re Rijckaert*, 9 F.3d 1531, 1534 (Fed. Cir. 1993). "That which may be inherent is not necessarily known. Obviousness cannot be predicated on what is unknown," even if the inherency of a certain feature is later established. *Id.*

As discussed above, none of the cited references teaches or suggests introduction and expression of a yeast RHO gene, such as that shown in SEQ ID NO: 1, in plants would confer an increase in the amount of a fine chemical that is not the encoded protein. Thus, the ability to confer an increase in the amount of a fine chemical that is selected from the group consisting of amino acids, carbohydrates, vitamins, organic acids, fatty acids, and carotenoids when expressed in plants is a property of the RHO gene that was not known prior to the present application. The Examiner has not provided any rationale or evidence making clear that the missing descriptive matters (i.e. increase the amount of a fine chemical that is not the encoded protein) are necessarily present in the thing described in the references (i.e. the yeast RHO gene). Because no rationale or evidence has been provided, a *prima facie* case of obviousness has not been established. For this additional reason, the rejection should be withdrawn.

For at least the above reasons and further in view of the present amendment, Applicants respectfully submit that the cited references, alone or in combination, do not render the claimed subject matter obvious. Accordingly, reconsideration and withdrawal of the rejection is respectfully requested.

## CONCLUSION

For at least the above reasons, Applicants respectfully request withdrawal of the rejections and allowance of the claims. If any outstanding issues remain, the Examiner is invited to telephone the undersigned at the number given below.

Applicants reserve all rights to pursue the non-elected claims and subject matter in one or more divisional applications.

Accompanying this response is a petition for a three-month extension of time to respond to the Office Action mailed July 20, 2010 with the required fee authorization. No further fee is

believed due. However, if any additional fee is due, the Director is hereby authorized to charge our Deposit Account No. 03-2775, under Order No. 12810-00197-US from which the undersigned is authorized to draw.

Respectfully submitted,

By /Hui-Ju Wu/

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